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Clinical Communications: Adults

A Case of Leukocytoclastic Vasculitis Following SARS-COV-2 Vaccination

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Abstract—Background: Although vaccination against coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been proven generally safe, rare but potentially serious adverse reactions do occur. Leukocytoclastic vasculitis (LCV) is a small-vessel vasculitis that has been associated with other immunizations, but, to our knowledge, has not been previously reported in association with vaccines directed against SARS-CoV-2. **Case Report:** We report the case of a 22-year-old man with no known past medical history who presented to the Emergency Department with 2 days of migratory arthritis in his ankles and palpable purpura on his bilateral lower extremities, occurring 10 days after receiving the Johnson & Johnson SARS-CoV-2 vaccine. The patient's clinical presentation was suggestive of leukocytoclastic vasculitis, and this diagnosis was confirmed on skin biopsy. **Why Should an Emergency Physician Be Aware of This?** Recognition of vasculitides is important for timely treatment and prevention of complications. In a patient presenting with palpable purpura after immunization against SARS-CoV-2, LCV should be promptly considered and worked up by the Emergency Physician, though management is most often entirely outpatient and the clinical course is typically mild and self-resolving. © 2021 Elsevier Inc. All rights reserved.

Keywords—leukocytoclastic vasculitis; SARS-CoV-2; COVID; vaccine; Henoch-Schönlein Purpura

INTRODUCTION

Leukocytoclastic vasculitis (LCV) is a small-vessel vasculitis that is most commonly characterized by palpable purpura on the lower extremities. When occurring in chil-

dren in combination with abdominal pain, arthritis, or renal involvement, it is known as immunoglobulin A (IgA) vasculitis or Henoch-Schönlein purpura. In all its forms, the pathophysiology of LCV involves immune-complex deposition within small vessels, as well as activation of the complement system.

The etiology of LCV remains somewhat obscure, but like other vasculitides, a variety of genetic, environmental, and immune factors are thought to play a role. A number of specific inciting factors have been identified, including medications (especially antibiotics, nonsteroidal anti-inflammatory drugs [NSAIDs], and diuretics), microbial pathogens (hepatitis B virus, hepatitis C virus, human immunodeficiency virus [HIV], Epstein-Barr virus [EBV], and *streptococci*), malignancy, inflammatory bowel disease, and connective tissue diseases (systemic lupus erythematosus, Sjögren syndrome, rheumatoid arthritis). Case reports have demonstrated an association between vaccinations such as influenza and the development of LCV, and a single case-control study found a correlation between measles-mumps-rubella vaccination and an increased risk of Henoch-Schönlein purpura in children (1–4). In up to 50% of cases, no identifiable cause is found, and the vasculitis is considered idiopathic.

Much remains unknown about the effect of infection with SARS-CoV-2 on immune function. Severe cases of coronavirus disease 2019 (COVID-19) have been associated with dysregulation of both the innate and acquired immune system, and, indeed, there have been case reports of IgA vasculitis subtypes after COVID-19 infection.

RECEIVED: 27 May 2021; FINAL SUBMISSION RECEIVED: 27 July 2021;
 ACCEPTED: 12 October 2021

However, to date, we know of no previously reported case of LCV after vaccination against the SARS-CoV-2 virus.

CASE REPORT

A 22-year-old, previously healthy man presented to the Emergency Department (ED) with a chief complaint of ankle swelling and lower extremity rash. He had first noticed swelling and pain in his left ankle 2 days prior. Later that same day, he began to notice a purplish rash on the tops of his feet, spreading up toward his shins. The day prior to presentation, the swelling in his left ankle resolved, but his right ankle became swollen and painful. The rash had continued to spread, though it remained confined to his lower legs. He reported no other rash or bruising, no mucosal bleeding, and no fever, myalgias, fatigue, abdominal pain, or hematuria.

The patient had received the Johnson & Johnson SARS-CoV-2 vaccine 10 days earlier, and this was followed by 1 day of low-grade fever without associated symptoms. Aside from that, the patient had no recent history of illness other than some isolated rhinorrhea a month prior, which was not accompanied by fever, cough, or sore throat. Presentation was in May, outside of typical viral season in this ED. In addition, presentation was during the COVID-19 pandemic, when masks remained mandated and rates of influenza and other respiratory viruses were lower than baseline (5). The patient had no prior history of allergy or autoimmune disease and was taking no prescription or over-the-counter medications. He had no recent travel and no exposure to animals.

On examination, the patient appeared to be in no distress, was afebrile at 36.8°C, and was hemodynamically stable with a blood pressure of 129/83 mm Hg. He was initially tachycardic at 109 beats/min, but heart rate decreased to 79 beats/min with administration of NSAIDs for pain. He was noted to have scattered, violaceous, palpable purpura over the dorsal surfaces of both feet and the anterior aspects of both lower extremities distal to the knees. The largest lesion was 3 cm in diameter, all were non-blanching, and none were tender. His right ankle was swollen, tender, and erythematous, with pain upon active and passive range of motion. [Figure 1](#) is a representative photograph of the patient's lower extremities.

Laboratory data were notable for 1+ hematuria on urine dip, with 1 red blood cell/high-power field, 1 white blood cell/high-power field, and no bacteria in the urine sediment. Serum chemistries were notable for normal renal function, with a blood urea nitrogen of 9 mg/dL and a creatinine of 0.88 mg/dL. Complete blood count showed a mild leukocytosis at $10.3 \times 10^3/\text{mL}$, and normal platelets at $307 \times 10^3/\text{mL}$. Coagulation studies were within normal limits, with a prothrombin time of 14.1 s and a



Figure 1. Patient's lower extremities

partial thromboplastin time of 35.5 s. Dermatology was consulted and recommended a number of secondary laboratory studies, as well as biopsy to confirm diagnosis and to investigate possible triggers. They advised brief admission to ensure pain control and no acute worsening, but did not think it necessary for secondary laboratory data to result prior to discharge, as LCV can most often be managed as an outpatient even on first presentation. Notable laboratory data that resulted post-discharge included a decreased C3 at 61 mg/dL, a negative antineutrophil cytoplasmic antibodies test (ANCA), a borderline elevated rheumatoid factor of 16 IU/mL, and an elevated antistreptolysin-O (ASO) antibody titer of 944. Cytomegalovirus (CMV) IgG was positive, CMV IgM was negative, and EBV and HIV antibodies were negative. A SARS-CoV-2 polymerase chain reaction test was negative.

Biopsy of the lesions showed perivascular and interstitial neutrophilic infiltrate with eosinophils. Immunofluorescence was performed, which demonstrated perivascular deposition of IgA and C3, and IgG. The final pathology report, which resulted 1 week after discharge, read, in part: "in the context of the immunofluorescence findings, the appearance is most suggestive of leukocytoclastic vasculitis. Clinical correlation is needed to determine the etiology." Patient was followed up in the Dermatology clinic for biopsy-proven LCV; per chart review, rash and swelling were noted to be improving.

DISCUSSION

In a patient presenting to the ED with purpura, the differential diagnosis includes conditions ranging from the life-threatening (e.g., meningococcemia, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura) to the relatively benign (e.g., immune thrombocytopenia) (6). Purpura that are non-palpable are most often associated with pathologies of thrombocytopenia. In a patient with normal platelets and coagulation studies and the presence of other signs and symptoms such as migratory arthritis and microscopic hematuria, the likelihood of vasculitis is high. A variety of small-vessel vasculitides present with dermatologic manifestations including palpable purpura, and associated symptoms can assist in creating a differential. IgA vasculitis, a form of LCV, can present with arthritis and renal disease. Eosinophilic granulomatosis with polyangiitis and granulomatosis with polyangiitis often present with sinusitis and some form of lung involvement, and are associated with ANCA positivity. Polyarteritis nodosa, which is typically classified as a medium-vessel disease but can cause purpura, often manifests with gastrointestinal symptoms, renal disease, and neuropathy.

The classic presentation of LCV is one of palpable purpura appearing on the lower legs, as was seen in this patient. The lesions are typically painless but are sometimes pruritic or mildly painful. Patients with the IgA subtype of LCV classically present with migratory arthralgias or arthritis, or renal involvement with hematuria, as was also seen in this patient. Identifiable triggers for LCV—which may include medications, viral or other infections, and possibly, vaccinations—tend to occur 7–10 days prior to the development of cutaneous findings, which would be consistent with the time course seen in this case if the SARS-CoV-2 vaccine was, in fact, the inciting cause. This patient did have a positive ASO titer, suggesting streptococcal infection as one other possible trigger, but did not have a recent history of an upper respiratory infection, sore throat, or skin infection.

The vaccines developed for SARS-CoV-2 elicit responses from the innate immune system as well as the adaptive immune system (T lymphocytes and B lymphocytes), resulting in the production of both cytokines and antibodies (7). The Johnson & Johnson vaccine delivers SARS-CoV-2 spike protein genetics on an Ad26 adenovirus vector, which is highly immunogenic (8). Adenovirus triggers cytokine release, including interleukin (IL)-6, IL-12, and tumor necrosis factor- α , as well as antibody production and T-cell activation (9). An overzealous immunologic response could plausibly result in the formation of aberrant antibody complexes and infiltration of neutrophils in and around small vessel walls.

The clinical course of LCV is typically mild and self-resolving, and in the absence of systemic complications (e.g., nephritis), supportive care is generally all that is required. Rest, leg elevation, and compression stockings are often recommended, given the tendency for lesions to develop in dependent areas. NSAIDs can be utilized for pain management, and antihistamines for pruritis (10,11). Glucocorticoids can be utilized if the disease course is prolonged, although data supporting the use of corticosteroids come only from case reports. In adults with IgA nephritis, glucocorticoids are recommended if there is elevated serum creatinine, proteinuria of more than 1 g per day, or biopsy-proven kidney involvement (12). Patients with arthritis generally respond well to NSAID therapy, but glucocorticoid therapy can be effective for persistent pain.

WHY SHOULD AN EMERGENCY PHYSICIAN BE AWARE OF THIS?

As a large fraction of the population undergoes vaccination against SARS-CoV-2, emergency physicians may see rare adverse reactions potentially associated with immune dysregulation, such as LCV. Though the condition itself is rarely life threatening, patients with suspected LCV can benefit from prompt recognition, identification of a recent or current trigger, and assessment for and management of associated symptoms.

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